

CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

22-474

Trade Name: ella 30mg Tablet

Generic Name: ulipristal acetate

Sponsor: Laboratoire HRA Pharma

Approval Date: August 13, 2010

Indications: For the prevention of pregnancy following unprotected intercourse or a known or suspected contraceptive failure. ella is not intended for routine use as a contraceptive.

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APPROVAL LETTER



NDA 022474

NDA APPROVAL

Laboratoire HRA Pharma
C/o Target Health, Inc.
Attention: Glen D. Park, Pharm.D.
Senior Director, Clinical and Regulatory Affairs
261 Madison Avenue, 24th Floor
New York, NY 10016

Dear Mr. Park:

Please refer to your New Drug Application (NDA) dated October 14, 2009, received October 15, 2009, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for **ella** (ulipristal acetate) 30 mg tablet.

We acknowledge receipt of your amendments dated October 27, November 6, 17, 30, December 14, 2009, January 19, February 16, 25, March 16, April 6, May 7, 14, June 29, July 9 and August 12, 2010.

This new drug application provides for the use of **ella** (ulipristal acetate) 30 mg tablet for the prevention of pregnancy following unprotected intercourse or a known or suspected contraceptive failure. **ella** is not intended for routine use as a contraceptive.

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling text.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit, via the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format, as described at <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>, that is identical to the enclosed labeling text for the package insert. Information on submitting SPL files using eLIST may be found in the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As" at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf>.

The SPL will be accessible via publicly available labeling repositories.

CARTON AND IMMEDIATE CONTAINER LABELS

Submit final printed carton and container labels that are identical to the carton and immediate container labels submitted on May 14, 2010 as soon as they are available, but no more than 30 days after they are printed. Please submit these labels electronically according to the guidance for industry titled "Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (June 2008)." Alternatively, you may submit 12 paper copies, with 6 of the copies individually mounted on heavy-weight paper or similar material. For administrative purposes, designate this submission "**Final Printed Carton and Container Labels for approved NDA 022474.**" Approval of this submission by FDA is not required before the labeling is used.

Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are waiving the pediatric study requirement for pre-menarcheal patients because pre-menarcheal patients are not at risk of becoming pregnant and the use of this product before menarche is not indicated. We note that you have fulfilled the pediatric study requirement for post-menarcheal pediatric patients by extrapolation of adult data.

POSTMARKETING REQUIREMENTS UNDER 505(o)

Section 505(o)(3) of the FDCA authorizes FDA to require holders of approved drug and biological product applications to conduct postmarketing studies and clinical trials for certain purposes, if FDA makes certain findings required by the statute.

We have determined that an analysis of spontaneous postmarketing adverse events reported under subsection 505(k)(1) of the FDCA will not be sufficient to identify any unexpected serious risks of adverse maternal, fetal or neonatal outcomes following exposure to ulipristal acetate during pregnancy, or adverse events associated with use of ulipristal acetate by adolescents, particularly with respect to alterations in the menstrual cycle.

Furthermore, the new pharmacovigilance system that FDA is required to establish under section 505(k)(3) of the FDCA has not yet been established and is not sufficient to identify these serious risks.

Therefore, based on appropriate scientific data, FDA has determined that you are required to conduct the following:

1673-1. A prospective, observational pregnancy outcome study to include fetal and neonatal outcomes and maternal pregnancy complications following a pregnancy exposed to ulipristal acetate (e.g., in case of inadvertent administration to a woman with an unrecognized pregnancy, or in case of emergency contraceptive failure). This study may be conducted by adding a US component to your planned European pregnancy outcome study.

The timetable you submitted on August 12, 2010, states that you will conduct this study according to the following timetable:

Final Protocol Submission:	February 13, 2011
Study Completion Date:	December 31, 2013
Final Report Submission:	June 30, 2014

1673-2. A case-control study of pregnancy loss complications. This study will be conducted as an expansion of the pregnancy outcome study (described under 1673-1), if a signal of concern regarding pregnancy complications is found in that study.

The timetable you submitted on August 12, 2010, states that you will conduct this study according to the following schedule:

Final Protocol Submission:	February 13, 2011
Study Completion Date:	December 31, 2014
Final Report Submission:	June 30, 2015

1673-3. An observational study in adolescents, with particular focus on alterations to the menstrual cycle after use of ulipristal acetate. This study may be conducted by adding a US component to your planned UK/Sweden study of use in adolescents. The study should enroll at least 50 subjects (completers) under the age of 16 over the full study (these do not necessarily have to be US subjects).

The timetable you submitted on August 12, 2010, states that you will conduct this study according to the following schedule:

Final Protocol Submission:	February 13, 2011
Study Completion Date:	April 30, 2012
Final Report Submission:	October 30, 2012

Finally, we have determined that only a clinical trial (rather than a nonclinical or observational study) will be sufficient to assess an unexpected serious risk of drug transfer from mother to child in lactating women.

Therefore, based on appropriate scientific data, FDA has determined that you are required to conduct the following:

1673-4. A pharmacokinetic trial in lactating women, with evaluation of the rate and extent of excretion of ulipristal acetate and its active metabolite into breast milk. Your planned lactation trial to be conducted in Chile appears likely to fulfill this requirement.

The timetable you submitted on August 12, 2010, states that you will conduct this trial according to the following schedule:

Final Protocol Submission:	October 13, 2010
Trial Completion Date:	October 13, 2011
Final Report Submission:	April 30, 2012

Submit all protocols to your IND 49,381 with a cross-reference letter to this NDA 22-474. Submit all final reports to your NDA. Prominently identify the submission with the following wording in bold capital letters at the top of the first page of the submission, as appropriate:

- **REQUIRED POSTMARKETING PROTOCOL UNDER 505(o)**
- **REQUIRED POSTMARKETING FINAL REPORT UNDER 505(o)**
- **REQUIRED POSTMARKETING CORRESPONDENCE UNDER 505(o)**

Section 505(o)(3)(E)(ii) of the FDCA requires you to report periodically on the status of any study or clinical trial required under this section. This section also requires you to periodically report to FDA on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Section 506B of the FDCA, as well as 21 CFR 314.81(b)(2)(vii) requires you to report annually on the status of any postmarketing commitments or required studies or clinical trials.

FDA will consider the submission of your annual report under section 506B and 21 CFR 314.81(b)(2)(vii) to satisfy the periodic reporting requirement under section 505(o)(3)(E)(ii) provided that you include the elements listed in 505(o) and CFR 314.81(b)(2)(vii). We remind you that to comply with 505(o), your annual report must also include a report on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Failure to submit an annual report for studies or clinical trials required under 505(o) on the date required will be considered a violation of FDCA section 505(o)(3)(E)(ii) and could result in enforcement action.

POSTMARKETING COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitment in your submission dated August 12, 2010. This commitment is listed below.

1673-5. To conduct an in vivo drug-drug interaction trial of ulipristal acetate with a CYP3A4 inducer.

Final Protocol Submission: February 13, 2011
Trial Completion: February 13, 2013
Final Report Submission: August 13, 2013

Submit clinical protocols to your IND 49,381 for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii) you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies/trials, number of patients entered into each study/trial. All submissions, including supplements, relating to these postmarketing commitments should be prominently labeled “**Postmarketing Commitment Protocol**,” “**Postmarketing Commitment Final Report**,” or “**Postmarketing Commitment Correspondence**.”

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705-1266

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the package insert, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. For instruction on completing the Form FDA 2253, see page 2 of the Form. For more information about submission of promotional materials to the Division of Drug Marketing, Advertising, and Communications (DDMAC), see <http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm>.

LETTERS TO HEALTH CARE PROFESSIONALS

If you decide to issue a letter communicating important safety-related information about this drug product (i.e., a “Dear Health Care Professional” letter), we request that you submit, at least 24 hours prior to issuing the letter, an electronic copy of the letter to this NDA, to CDERMedWatchSafetyAlerts@fda.hhs.gov, and to the following address:

MedWatch Program
Office of Special Health Issues
Food and Drug Administration
10903 New Hampshire Ave
Building 32, Mail Stop 5353
Silver Spring, MD 20993

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

MEDWATCH-TO-MANUFACTURER PROGRAM

The MedWatch-to-Manufacturer Program provides manufacturers with copies of serious adverse event reports that are received directly by the FDA. New molecular entities and important new biologics qualify for inclusion for three years after approval. Your firm is eligible to receive copies of reports for this product. To participate in the program, please see the enrollment instructions and program description details at <http://www.fda.gov/Safety/MedWatch/HowToReport/ucm166910.htm>.

POST-ACTION FEEDBACK MEETING

New molecular entities and new biologics qualify for a post-action feedback meeting. Such meetings are used to discuss the quality of the application and to evaluate the communication process during drug development and marketing application review. The purpose is to learn from successful aspects of the review process and to identify areas that could benefit from improvement. If you would like to have such a meeting with us, call the Regulatory Project Manager for this application.

If you have any questions, please call Pamela Lucarelli, Regulatory Health Project Manager, at (301) 796-3961.

Sincerely,

Julie Beitz, M.D.
Director
Office of Drug Evaluation III
Center for Drug Evaluation and Research

Enclosure: Content of Labeling